REMARKS

A check in the amount of $ 205 for two month Extension of Time (small entity) is enclosed. Any fees that may be due in connection with the filing of this paper, if the attached check is in the wrong amount, improper or is missing, or with this application during its entire pendency, may be charged to Deposit Account No. 50-1213. If a Petition for an Extension of Time is required, this paper is to be considered such petition.

Claims 1-30 are pending in this application. Claims 9-16 are withdrawn from consideration. Claims 1, 2, 6, 7, 8, 17-20 and 24 and the specification are amended herein to correct obvious typographical errors.

A supplemental Information Disclosure Statement is being sent under separate cover.

RESTRICTION REQUIREMENT AND PREVIOUS RESPONSE

Applicant notes that the Office Action does not address Applicant's traversal of the previous Restriction Requirement. While not agreeing with the propriety of the Restriction Requirement, in the interest of advancing the prosecution of the application, Applicant hereby withdraws traversal of same. Applicant's previous election of group I is made without traverse.

REJECTION OF CLAIMS 1-8 AND 17-30 UNDER 35 U.S.C. § 112, FIRST PARAGRAPH FOR ALLEGED LACK OF ENABLEMENT

Claims 1-8 and 17-30 are rejected under 35 U.S.C. § 112, first paragraph because the specification, while being enabling for certain disorders associated with amyloid protein deposits, allegedly does not reasonably provide enablement for the broad phrase of amyloidosis. The Office Action alleges that the specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims. The Office Action urges that the specification fails to provide information that would allow the skilled artisan to practice the instantly claimed subject matter without undue experimentation. It is further urged that the application allegedly fails to set forth the

criteria that define "amyloidosis" and does not provide information allowing the skilled artisan to ascertain the conditions associated with "amyloidosis". The Office Action alleges that a limited number of conditions associated with amyloidosis are set forth in the application. It is alleged that the specification fails to provide sufficient working examples. The Office Action further urges that the specification also fails to support the treatment for Alzheimer. The Office Action concludes that the instant claims read on all conditions covered under the broad phrase of "amyloidosis" but the specification allegedly fails to provide information sufficient to practice the claimed subject matter without undue experimentation. Applicant respectfully traverses this rejection.

Relevant Law

To satisfy the enablement requirement of 35 U.S.C § 112, first paragraph, the specification must teach one of skill in the art to make and use the invention without undue experimentation. *Atlas Powder Co. v. E.I. DuPont de Nemours*, 750 F.2d 1569, 224 USPQ 409 (1984). This requirement can be met by providing sufficient disclosure, either through illustrative examples or terminology, to teach one of skill in the art how to make and how to use the claimed subject matter without undue experimentation. This clause does not require "a specific example of everything *within the scope* of a broad claim." *In re Anderson*, 176 USPQ 331, at 333 (CCPA 1973), emphasis in original. Rather, the requirements of § 112, first paragraph "can be fulfilled by the use of illustrative examples **or** by broad terminology." *In re Marzocchi et al.*, 469 USPQ 367 (CCPA 1971)(emphasis added).

Further, because "it is manifestly impracticable for an applicant who discloses a generic invention to give an example of every species falling within it, or even to name every such species, it is sufficient if the disclosure teaches those skilled in the art what the invention is and how to practice it." *In re Grimme, Keil and Schmitz*, 124 USPQ 449, 502 (CCPA 1960). Thus, there is no doubt that a patentee's invention may be broader than the particular embodiment shown in the specification. A patentee not only is entitled to narrow claims particularly directed to the preferred

embodiment, but also to broad claims that define the invention without a reference to specific instrumentalities. *Smith v. Snow*, 294 U.S. 1, 11, 24 USPQ 26, 30 (1935).

Thus, there is no requirement for disclosure of every species within a genus. Applicant is entitled to claims are commensurate in scope not only with what applicant has specifically exemplified, but commensurate in scope with that which one of skill in the art could obtain by virtue of that which the applicant has disclosed.

The inquiry with respect to scope of enablement under 35 U.S.C. §112, first paragraph, is whether it would require undue experimentation to make and use the claimed invention. A considerable amount of experimentation is permissible, particularly if it is routine experimentation. The amount of experimentation that is permissible depends upon a number of factors, which include: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, and the breadth of the claims. *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int'f 1986); see also *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988).

PTO GUIDELINES

The standard for determining whether the specification meets the enablement requirement is whether it enables any person skilled in the art to make and use the claimed subject matter without **undue** experimentation. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400 (Fed. Cir. 1999) (emphasis added). In determining whether any experimentation is "undue," the above-noted factors are to be considered.

As instructed in the published PTO guidelines, it is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others. The analysis must consider all the evidence related to each of the factors, and any conclusion of non-enablement must be based on the evidence as a whole. *Id.* 8 USPQ2d at 1404 & 1407.

The starting point in an evaluation of whether the enablement requirement is satisfied is an analysis of each claim to determine its scope. As set forth in the

guidelines, all questions of enablement are evaluated against **the claimed subject matter**. The focus of the inquiry is whether everything within the scope of the claim is enabled. With respect scope of enablement, the only relevant concern should be whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims. *In re Moore,* 439 F.2d 1232, 169 USPQ 236 (CCPA 1971). Once the scope of the claims is addressed, a determination must be made as to whether one skilled in the art is enabled to make and use the entire scope of the claimed subject matter without undue experimentation.

Analysis

Applying the above factors to the instant claims, applicant respectfully submits that, as described in detail below, it would not require undue experimentation to practice the full scope of the claimed subject matter.

Scope of the claims

Applicant respectfully submits that claims 1-8 and 17-30 are directed towards methods for treating amyloidosis and drug products for treatment of amyloidosis as follows: Claim 1 is directed to a method of treating amyloidosis in a mammal suffering therefrom, comprising administration to the mammal of a therapeutically effective amount of an isolated pure compound selected from a group consisting of the compounds of formula A, formula B, formula C, formula D, and formula E as described therein. Claims 2-5 depend from claim 1 and further define the method. Claims 17-30 depend from claim 1 and further define the compounds of formulae A-E. Claim 6 is directed to a drug product for the treatment of amyloidosis in a mammal. Claims 7 and 8 depend from claim 6 and further define the drug product. The compounds used in the methods and drug products of the instant claims are described in detail in the application (see, *e.g.*, page 10, line 3 through page 12, line 29 and page 15, line 6 through page 16, line 13). The application describes amyloidosis (see, *e.g.*, page 1, line 10 through page 3, line 14) and various conditions associated with amyloidosis (see, *e.g.*, pages 1-6). Furthermore, as

discussed in detail below, there is a wealth of information available in the literature about amyloidosis and various disease conditions associated with amyloid deposition. Therefore, the scope of the claims is not broader than the application disclosure.

The level of skill in the art is high

The level of skill in this art is recognized to be high (see, e.g., Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int'f 1986)). In addition, the numerous articles and patents that are of record in this application that are authored by those of a high level of skill for an audience of a high level of skill further evidences the high level of skill in this art.

Knowledge of those of skill in the art

At the time of the effective filing date of this application and before, the skilled artisan knew various conditions associated with amyloid protein deposition. The articles cited in the specification, of record and attached hereto, describe amyloidosis in extensive details. For example, Gejyo *et al.* discuss various forms of amyloid and describe amyloidosis associated with hemodialysis in an article in *Biochem. Biophys. Res. Comm.*

Kamei *et al.*, in an article in *Acta Pathol. Jpn.*, describe amyloidosis associated with diseases in children. The article discusses chronic inflammatory diseases associated with amyloid deposition.

Tawara *et al.* have described conditions associated with amyloidosis in an article in *J. Lab. Clin. Med.*

Harada *et al.* have described diseases associated with amyloidosis and identification of major components of amyloid fibrils in an article in *J. Histochem. and Cytochem.*

Metaxas has described familial mediterranean fever associated with amyloidosis in an article in *Kidney Int.*

Benson *et al.* have reported amyloidosis associated with rheumatic and neoplastic disease.

Johnson *et al.* have described mechanism of amyloidosis in pancreatic islets.

Further, amyloidosis and various conditions associated with it are described in a large volume of literature not cited in the application. For example, U.S. Patent 5,981,168 describes that the term amyloidoses indicates a group of diseases whose common characteristic is the presence, in the extracellular space, of amyloid deposits. Amyloidogenic proteins are proteins that have the tendency to aggregate and precipitate as amyloid. Proteins that precipitate as amyloid are both normal proteins, or truncated forms thereof, and mutated proteins, where one or more of the amino acid residues occurring at certain positions of the normal protein sequence are replaced by a different amino acid. Amyloid deposits are composed of insoluble fibrils, also referred to as amyloid fibrils. Amyloid fibrils cause cellular degeneration and organ failure that, in turn, result in different pathologies depending on the tissues and organs involved. The reference further describes different types of amyloidotic diseases as systemic amyloidoses and amyloidoses of the peripheral and central nervous system. It further describes that amyloidoses of the central nervous system include, for example, Alzheimer's disease, Down Syndrome, spongiform encephalopathies such as Creutzfeld-Jacob disease and the like.

U.S. patent 5,869,469 describes amyloidosis as a pathological condition characterized by the presence of amyloid. Amyloid is a generic term referring to a group of diverse but specific extracellular protein deposits which are seen in a number of different diseases. Though diverse in their occurrence, all amyloid deposits have common morphologic properties, stain with specific dyes (e.g., Congo red), and have a characteristic red-green birefringent appearance in polarized light after staining. They also share common ultrastructural features and common x-ray diffraction and infrared spectra.

The reference further describes that amyloidosis can be classified clinically as primary, secondary, familial and/or isolated. Primary amyloidosis appears de novo without any preceding disorder. Secondary amyloidosis is that form which appears as a complication of a previously existing disorder. Familial amyloidosis is a

genetically inherited form found in particular geographic populations. Isolated forms of amyloidosis are those that tend to involve a single organ system. Different amyloids are also characterized by the type of protein present in the deposit. For example, neurodegenerative diseases such as scrapie, bovine spongiform encephalitis, Creutzfeldt-Jakob disease and the like are characterized by the appearance and accumulation of a protease-resistant form of a prion protein (referred to as AScr or PrP-27) in the central nervous system. Similarly, Alzheimer's disease, another neurodegenerative disorder, is characterized by congophilic angiopathy, neuritic plaques and neurofibrillary tangles, all of which have the characteristics of amyloids. In this case, the plaque and blood vessel amyloid is formed by the beta protein. Other systemic or localized diseases such as adult-onset diabetes, complications of long-term hemodialysis and sequelae of long-standing inflammation or plasma cell dyscrasias are characterized by the accumulation of amyloids systemically. In each of these cases, a different amyloidogenic protein is involved in amyloid deposition.

U.S. patent 5,972,956 describes amyloidosis and diseases associated as follows: Amyloid plaque formation is found in a number of diseases, including Alzheimer's disease, scrapie, bovine spongiform encephalophy, Gerstmann-Straussler Syndrome, and the like. The amyloid plaques comprise proteins bound together in a fibrillous matrix. Amyloidosis is the general name given to diseases and conditions characterized by the presence of amyloid protein. A number of different types of amyloid protein are known, and all types are considered pathological, since no normally occurring amyloids are known. Accordingly, the presence of amyloid protein in a host is an indication of abnormal formation of fibrils and plaques. Amyloidosis has been clinically observed in a number of disease states, including certain mental illnesses, neurological diseases, and collagenosis. Indeed, the brains of subjects diagnosed with Alzheimer's disease have one thing in common, namely an abundance of amyloid in the form of plaques and tangles.

U.S. patent 5,643,562 describes amyloidosis as a pathological condition

characterized by the presence of amyloid. Amyloid is a generic term referring to a group of diverse but specific extracellular protein deposits which are seen in a number of different diseases. Though diverse in their occurrence, all amyloid deposits have common morphologic properties, stain with specific dyes (e.g., Congo red), and have a characteristic red-green birefringent appearance in polarized light after staining. They also share common ultrastructural features and common x-ray diffraction and infrared spectra. It further discusses that amyloidosis various classes of amyloidosis and discloses that in different classes, a different amyloidogenic protein is invoived in amyloid deposition.

Hence, those of skill in the art are well- aware of amyloidosis and various conditions associated with it. Therefore, based on the teachings and guidance in the specification and the knowledge of those of skill in the art, one can readily recognize the conditions associated with amyloidosis and apply the methods claimed herein for treatment thereof.

The amount of direction and guidance presented, teachings in the specification

The application describes amyloid and amyloidosis in detail on pages 1-3 of the specification. Description of amyloid as a therapeutic target for Alzheimer's disease can be found in the specification on pages 4-6. The application describes on page 14, lines 13-24, that treatment of amyloidosis includes preventing the disease from occurring in a mammal that may be predisposed to the disease but does not yet experience or exhibit symptoms of the disease (prophylactic treatment), inhibiting the disease (slowing or arresting its development), providing relief from the symptoms or side-effects of the disease (including palliative treatment), and relieving the disease (causing regression of the disease). It is further disclosed that "treating" amyloidosis includes any one or more of the following: preventing, inhibiting, reducing, disassembling, disrupting, and disaggregating amyloid fibrils and amyloid protein deposits, such as Aβ and the other amyloids. The specification describes on page 16, lines 15-20, that compounds of the instantly claimed methods and drug

products act to inhibit or prevent amyloid fibril formation, inhibit or prevent amyloid fibril growth, and/or cause disassembly, disruption, and/or disaggregation of preformed amyloid fibrils and amyloid protein deposits. The *in vitro* methods to measure the activity these compounds are described in Examples 1 through 4, on pages 21-26 and Assay 1, on page 28. The specification on pages 28-29, also describes an *in vivo* assay (assay 2) to measure the activity of the compounds of instantly claimed methods and drug products against conditions associated with amyloidoses, such as Alzheimer's disease in humans. The exemplary embodiments described in the specification demonstrate disassembly/disruption of Alzheimer's disease Aβ 1-42 fibrils, dose-dependent disassembly/disruption of Alzheimer's disease Aβ 1-40 fibrils, disaggregation of Alzheimer's disease Aβ 1-40 fibrils, dose-dependent disaggregation of Alzheimer's disease Aβ 1-40 fibrils and disassembly/disruption of islet amyloid fibrils (amylin) by several compounds within the scope of instant claims. The specification also discloses that further *in vitro* and *in vivo* assays may be used to test the compounds for their effectiveness in the treatment of Alzheimer's disease, such as those described in European Published Patent Application No. 0 659 418. Based on the application disclosure and the exemplary embodiments in the application, a skilled artisan can easily apply the claimed methods for treating other conditions associated with amyloidosis. Therefore, the application provides sufficient guidance for one of skill in the art to make and use the full scope of the claimed subject matter.

Presence of working examples

The application provides several working examples to demonstrate the instantly claimed methods of treating amyloidosis. The application provides working examples where the instantly claimed method is demonstrated for the treatment of exemplary conditions associated with amyloidosis, such as Alzheimer's disease and type II diabetes. Working examples 1-4 in the specification illustrate disassembly/disruption of Alzheimer's disease Aβ 1-42 fibrils by the compounds used in the instantly-claimed methods and drug products, dose-dependent

disassembly/disruption of Alzheimer's disease Aβ 1-40 fibrils by tannic acid and gallic acid which are within the scope of the compounds used in the instant claims, disaggregation of Alzheimer's disease Aβ 1-40 fibrils by the compounds used in the instantly-claimed methods and drug products, dose-dependent disaggregation of Alzheimer's disease Aβ 1-40 fibrils by tannic acid and gallic acid which are within the scope of the compounds used in the instant claims. The specification demonstrates the application of instantly claimed methods for treating type II diabetes in example 5. Further, the specification also provides *in vitro* and *in vivo* assays to test the compounds for their effectiveness in the treatment of Alzheimer's disease.

Conclusion

In light of the scope of the claims, the description in the application, the high level of skill of those in this art, and the extensive knowledge of those of skill in this art, it would not require undue experimentation to practice full scope of the claims.

Examiner is reminded that applicant is entitled to claims that are commensurate in scope not only with what applicant has specifically exemplified, but commensurate in scope with that which one of skill in the art could obtain by virtue of that which the applicant has disclosed. It would be unfair and unduly limiting to require applicant to limit the claims to the exemplified methods of treating Alzheimers and type II diabetes when the specification clearly places those of skill in the art in possession of methods of treating other conditions associated with amyloidosis as instantly claimed. Therefore, it would be unfair, unduly limiting and contrary to the public policy upon which the U.S. patent laws are based to require applicant to limit the claims only to the exemplified species:

See, e.g., In re Goffe, 542 F.2d 801, 166 USPQ 85 (CCPA 1970):

> for the Board to limit appellant to claims involving the specific materials disclosed in the examples so that a competitor seeking to avoid infringing the claims can merely follow the disclosure and make routine substitutions "is contrary to the purpose for which the patent system exists - to promote progress in the useful arts".
>
> The public purpose on which the patent law rests requires the

> granting of claims commensurate in scope with the invention disclosed. This requires as much the granting of broad claims on broad inventions as it does the granting of more specific claims on more specific inventions" In re Sus and Schafer, 49 CCPA 1301, 306 F.2d 494, 134 USPQ 301, at 304.

To require applicant to limit the claims to only the exemplified species would permit those of skill in the art to practice what is disclosed in the application, but avoid infringing such limited claims. One of skill in the art could readily apply the exemplified methods to other conditions associated with amyloid deposition as taught in the specification. The first paragraph of §112 requires only that the disclosure be sufficient to teach one of skill in the art how to make and use the claimed subject matter without undue experimentation. As discussed above, the specification discloses various conditions associated with amyloid deposition and describes exemplary methods in detail. Based upon the disclosure in the application, those skilled in the art can use the methods as claimed.

Further, a patentee not only is entitled to narrow claims particularly directed to a specific embodiment, but also to broad claims that define an invention without a reference to specific instrumentalities. *Smith v. Snow*, 294 U.S. 1, 11, 24 USPQ 26, 30 (1935). As discussed above, applicant has described the conditions associated with amyloid deposition and exemplified methods for treatment thereof. Based on this disclosure, a person of skill in the art can practice the methods within the scope of instant claims.

As discussed above, the instant specification discloses the conditions associated with amyloid deposition and describes application of the instantly claimed method to exemplary conditions associated with amyloid deposition. A skilled artisan, with little experimentation, could apply the methods to other conditions that are associated with amyloid deposition and well recorded in the art and described in the specification. Therefore, the specification is enabling for the full scope of the claimed methods and drug products.

Rebuttal to Specific Arguments in the Office Action

Applicant herein provides response to the specific issues raised in the office action.

1. Criteria that define "amyloidosis"

The Office Action alleges that applicant fails to set forth the criteria that define "amyloidosis". Applicant strongly disagrees with this allegation.

As discussed above, amyloidosis is well defined in the art as a pathological condition characterized by the presence of amyloid. A person of skill in the art knew before the filing date of the application, various conditions associated with amyloidosis. Further, the application describes in detail amyloid and amyloidosis. For example, the specification on page 1, lines 11-19 describes characterstics of amyloids as follows:

> Amyloid is a generic term referring to a group of diverse but specific extracellular protein deposits which all have common morphological properties, staining characteristics, and X-ray diffraction spectra. Regardless of the nature of the amyloid protein deposited all amyloids have the following characteristics: 1) showing an amorphous appearance at the light microscopic level, appearing eosinophilic using hematoxylin and eosin stains; 2) staining with Congo red and demonstrating a red/green birefringence as viewed under polarized light (Puchtler et al., *J. Histochem. Cytochem.* 10:355-364, 1962), 3) containing a predominant beta-pleated sheet secondary structure, and 4) ultrastructurally consisting of non-branching fibrils of indefinite length and with a diameter of 7-10 nm.

Further, the application discloses on page 1, line 19, through page 2, line 6, various diseases associated with the amyloid protein deposition as follows:

> Amyloidoses today are classified according to the specific amyloid protein deposited. The amyloids include, but are not limited to, the amyloid associated with Alzheimer's disease, Down's syndrome and hereditary cerebral hemorrhage with amyloidosis of the Dutch type (where the specific amyloid is referred to as beta-amyloid protein or Aâ), the amyloid associated with chronic inflammation, various forms of malignancy and familial Mediterranean fever (where the specific amyloid is referred to as AA amyloid or inflammation-associated amyloid), the amyloid associated with multiple myeloma and other B-

cell dyscrasias (where the specific amyloid is referred to as AL amyloid), the amyloid associated with type II diabetes (where the specific amyloid is referred to as amylin or islet amyloid), the amyloid associated with the prion diseases including Creutzfeldt-Jakob disease, Gerstmann-Straussler syndrome, kuru, and scrapie (where the specific amyloid is referred to as PrP amyloid), the amyloid associated with long-term hemodialysis and carpal tunnel syndrome (where the specific amyloid is referred to as beta$_2$-microglobulin amyloid), the amyloid associated with senile cardiac amyloid and familial amyloidotic polyneuropathy (where the specific amyloid is referred to as prealbumin or transthyretin amyloid), and the amyloid associated with endocrine tumors such as medullary carcinoma of the thyroid (where the specific amyloid is referred to as variants of procalcitonin).

The application describes systemic amyloids on page 2, line 20, through page 3, line 14:

Systemic amyloids which include the amyloid associated with chronic inflammation, various forms of malignancy and familial Mediterranean fever (i.e. AA amyloid or inflammation-associated amyloidosis) (Benson and Cohen, *Arth. Rheum.* 22:36-42, 1979; Kamei et al, *Acta Path. Jpn.* 32:123-133, 1982; McAdam et al., *Lancet* 2:572-573, 1975; Metaxas, *Kidney Int.* 20:676-685, 1981), and the amyloid associated with multiple myeloma and other B-cell dyscrasias (i.e. AL amyloid) (Harada et al., *J. Histochem. Cytochem.* 19:1-15, 1971), as examples, are known to involve amyloid deposition in a variety of different organs and tissues generally lying outside the central nervous system. Amyloid deposition in these diseases may occur, for example, in liver, heart, spleen, gastrointestinal tract, kidney, skin, and/or lungs (Johnson et al, N. Engl. J. Med. 321:513-518, 1989). For most of these amyloidoses, there is no apparent cure or effective treatment and the consequences of amyloid deposition can be detrimental to the patient. For example, amyloid deposition in the kidney may lead to renal failure, whereas amyloid deposition in the heart may lead to heart failure. For these patients, amyloid accumulation in systemic organs leads to eventual death generally within 3-5 years. Other amyloidoses may affect a single organ or tissue such as observed with the Aâ amyloid deposits found in the brains of patients with Alzheimer's disease and Down's syndrome: the PrP amyloid deposits found in the brains of patients with Creutzfeldt-Jakob disease, Gerstmann-Straussler syndrome, and kuru; the islet amyloid (amylin) deposits found in the islets of Langerhans in the pancreas of 90% of patients with type II diabetes (Johnson et al, *N. Engl. J. Med.* 321:513-518, 1989; *Lab.*

Invest. 66:522 535, 1992); the beta$_2$-microglobulin amyloid deposits in the medial nerve leading to carpal tunnel syndrome as observed in patients undergoing long-term hemodialysis (Geyjo et al, *Biochem. Biophys. Res. Comm.* 129:701-706, 1985; *Kidney Int.* 30:385-390, 1986); the prealbumin/transthyretin amyloid observed in the hearts of patients with senile cardiac amyloid; and the prealbumin/transthyretin amyloid observed in peripheral nerves of patients who have familial amyloidotic polyneuropathy (Skinner and Cohen, *Biochem. Biophys. Res. Comm.* 99:1326-1332, 1981; Saraiva et al, *J. Lab. Clin. Med.* 102:590-603, 1983; *J. Clin. Invest.* 74:104-119, 1984; Tawara et al, *J. Lab. Clin. Med.* 98:811-822, 1989).

The application further describes Alzheimer's disease as an exemplary condition associated with amyloid deposition on page 3, line 16, through page 6, line 5. Thus, the application clearly sets forth the criteria that define "amyloidosis".

2. Conditions associated with amyloidosis

The Office Action alleges that the applicant fails to provide information allowing the skilled artisan to ascertain the conditions associated with "amyloidosis". Applicant disagrees.

As discussed above, the application provides detailed description of conditions associated with "amyloidosis" in the specification on pages 1-3. Furthermore, as shown by the articles cited in the application and provided herein, conditions associated with "amyloidosis" are well recorded in the literature. Therefore, based on the application disclosure and knowledge available in the art, a skilled artisan can easily recognize know the conditions associated with "amylo idosis".

3. Working examples

The Office Action further alleges that only a limited number of conditions associated with amyloidosis are set forth and application fails to provide sufficient working examples. Applicant disagrees.

As discussed above, the applications discusses various conditions associated with amyloid deposition on pages 1-3. The application provides working examples where the instantly claimed method is demonstrated for the treatment of exemplary

conditions associated with amyloidosis, such as Alzheimer's disease and type II diabetes. Working examples 1-4 in the specification illustrate disassembly/disruption of Alzheimer's disease Aβ 1-42 fibrils by polyhydroxylated aromatic compounds, dose-dependent disassembly/disruption of Alzheimer's disease Aβ 1-40 fibrils by tannic acid and gallic acid, disaggregation of Alzheimer's disease Aβ 1-40 fibrils by polyhydroxylated aromatic compounds, dose-dependent disaggregation of Alzheimer's disease Aβ 1-40 fibrils by tannic acid and gallic acid. The specification demonstrates the application of instantly claimed methods for treating type II diabetes in example 5. Based on this disclosure, a person of skill in the art can readily apply the instantly claimed methods for the treatment of other conditions associated with amyloidosis because the application teaches the conditions associated with amyloidosis, the method of treating the conditions and the assays to monitor the effect of treatment on the condition.

4. Support for the treatment of Alzheimer's disease

The Office Action alleges that the specification fails to support the treatment of Alzheimer's disease. Applicant disagrees.

The application describes amyloid as a therapeutic target for Alzheimer's disease on pages 4-6. The application provides working examples on pages 21-26, wherein treatment of Alzheimer's disease is achieved by disassembly/disruption of Alzheimer's disease Aβ 1-42 fibrils, dose-dependent disassembly/disruption of Alzheimer's disease Aβ 1-40 fibrils, disaggregation of Alzheimer's disease Aβ 1-40 fibrils, dose-dependent disaggregation of Alzheimer's disease Aβ 1-40 fibrils. Further, the application provides *in vitro* and *in vivo* assays on pages 28-29, to test the compounds for their effectiveness in the treatment of Alzheimer's disease. Therefore, the specification provides support for the treatment of Alzheimer's disease.

5. Information sufficient to practice the claimed subject matter

The Office Action alleges that the application fails to provide information sufficient to practice the claimed subject matter. Applicant disagrees.

As discussed above, the application describes conditions associated with amyloid depositions. There is a wealth of information available in the art about various conditions associated with amyloidosis. The application describes various compounds used in the instantly claimed methods and provides working examples where the method is applied within the scope of the instant claims for the treatment of Alzheimer's disease and type II diabetes. Based on this disclosure, a person of skill in the art can practice full scope of the instantly claimed subject matter.

REJECTION OF CLAIMS 6-8 UNDER 35 U.S.C. §102(b)

Claims 6-8 are rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Sawruk (U.S. Patent 5,478,579). The Office Action alleges that Sawruk teaches the use of myricetin in a pharmaceutical formulation for the treatment of osteoporosis. The Office Action urges that the use of an old composition for a new purpose does not create a patentably distinct composition. Reconsideration of the grounds for this rejection is respectfully requested in view of the following remarks.

Relevant law

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. In re Spada, 15 USPQ2d 1655 (Fed. Cir, 1990), In re Bond, 15 USPQ 1566 (Fed. Cir. 1990), Soundscriber Corp. v. U.S.. 360 F.2d 954, 148 USPQ 298, 301, adopted 149 USPQ 640 (Ct. Cl.) 1966. See, also, Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913,1920 (Fed. Cir.), cert. denied, 110 S.Ct. 154 (1989). "[A]ll limitations in the claims must be found in the reference, since the claims measure the invention". In re Lang, 644 F.2d 856, 862, 209 USPQ 288, 293 (CCPA 1981). Moreover it is incumbent on Examiner to identify wherein each and every facet of the claimed invention is disclosed in the reference. Lindemann Maschinen-fabrik Gmbh v. American Hoist and Derrick Co., 730 F.2d 1452, 221 USPQ 481 (Fed. Cir. 1984). Further, the reference must describe the invention as claimed sufficiently to have placed a person of ordinary skill in the art in possession of the invention. An inherent property has to flow naturally from what is taught in a reference In re Oelrich, 666 F.2d 578, 581, 212

USPQ 323, 326 (CCPA 1981).

Instant claims 6-8

Claim 6 is directed to a drug product for the treatment of amyloidosis in a mammal suffering therefrom, comprising ***a container labeled or accompanied by a label indicating that the drug product is for the treatment of amyloidosis,*** the container containing one or more dosage units each comprising at least one pharmaceutically acceptable excipient and, as an active ingredient, an isolated pure compound selected from the group consisting of the compounds of formula A, formula B, formula C, formula D, and formula E as described therein. Claims 7 and 8 depend from claim 6 and further define the drug product.

Disclosure of Sawruk and differences from the instant claims

Sawruk discloses a method for orally inducing and enhancing the absorption of calcium into mammalian bone tissue to thereby effect the ossification of such tissue by administering compositions comprising myricetin. The reference further discloses that such compositions are effective in the treatment of calcium deficiencies in mammalian bone. Further disclosed in the reference is a cost-effective method of strengthening human bone and related tissue, such as nails and teeth, using the herbal based medicinal composition disclosed therein. The reference does not disclose that the compositions can be used for the treatment of amyloidosis.

Since, Sawruk does not mention amyloidosis, it cannot disclose ***a drug product including a label*** stating that the compound is for treating amyloidosis. Instant claim 6 is directed to a combination of (i) a container labeled or accompanied by a label indicating that the drug product is for the treatment of amyloidosis, the container containing one or more dosage units each comprising at least one pharmaceutically acceptable excipient and, (ii) as an active ingredient, an isolated pure compound selected from the group consisting of the compounds of formula A, formula B, formula C, formula D, and formula E. Sawruk does not disclose this

combination, and thus does not anticipate the claims. The packaging material and label are not to be ignored simply because the printed matter is nonstatutory subject matter, but rather the functional relationship between the label and the substrate render the resulting article of manufacture new and unobvious. As stated in *In re Miller*, 164 USPQ 46 (CCPA 1969), "printed matter, in an article of manufacture claim, can be given 'patentable weight'." The court also stated that "what is significant here is not structural but functional relationship..." In *In re Gulack*, 217 USPQ 401 (CAFC 1983), the court stated that differences between an invention and the prior art cited against it cannot be ignored merely because those differences reside in the content of the printed matter.

In this instance, the label indicates that the drug product is to be used for treating amyloidosis. Therefore, there exists a new relationship between the label and the drug product. Sawruk does not disclose a drug product for the treatment of amyloidosis in a mammal suffering therefrom, containing a container labeled or accompanied by a label indicating that the drug product is for the treatment of amyloidosis. Thus, instant claims 6-8 are not anticipated by the disclosure of Sawruk.

In view of the above, reconsideration and allowance of the application are respectfully requested.

Respectfully Submitted,
Heller Ehrman White & McAuliffe LLP

Dale L. Rieger
Registration No. 43,045

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Address all correspondence to:
Stephanie Seidman, Esq.
HELLER EHRMAN WHITE & McAULIFFE LLP
4350 La Jolla Village Drive, 7th Floor
San Diego, California 92122
Telephone: 858-450-8400
Facsimile: 858-587-5360
e-mail: sseidman@hewm.com